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(+)-2-(1,2,3,4,4a,5,6,7-Octahydro-4a,8-dimethyl-7-oxo-2-naphthyl)-propionic acid: catemeric hydrogen bonding in a bicyclic sesquiterpenoid keto acid

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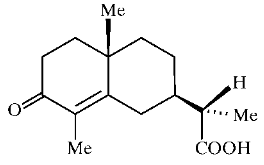
The title compound, $C_{15}H_{22}O_3$, derived from a naturally occurring sesquiterpenoid, has two molecules in the asymmetric unit, differing principally in the rotational conformation of the carboxyl group. Each species aggregates separately as a carboxyl-to-ketone hydrogen-bonding catemer [O···O = 2.752 (4) and 2.682 (4) Å, and O—H···O = 161 (4) and 168 (4)°], producing two crystallographically independent single-strand hydrogen-bonding helices, with opposite end-to-end orientations, passing through the cell in the *b* direction. Three intermolecular C—H···O═C close contacts exist for the ketone.

Comment

Our crystallographic studies of keto carboxylic acids explore the molecular characteristics that control their hydrogen-bonding patterns. Functionally unelaborated acids commonly aggregate in the solid as dimers, rarely as catemers (chains). An added ketone function provides opportunities for at least three additional hydrogen-bonding modes, the commonest of which, the acid-to-ketone catemer, forms a sizable overall minority of keto acid hydrogen-bonding cases. As we have previously suggested, carboxyl dimerization is suppressed in mono-enantiomeric species (Lalancette *et al.*, 1998) and also as a result of the presence of conformational restrictions (Brunskill *et al.*, 1999). In the presence of such molecular features, catemer formation may become the dominant hydrogen-bonding mode (Brunskill *et al.*, 1997).

The title compound, (I), derived from a sesquiterpenoid isolate of Artemisia, is a bicyclic ζ-keto acid, present as a single enantiomer. We have previously (Brunskill *et al.*, 2001) described a related diketo–dienoic acid (plus its hydrate) and Khanina *et al.* (1998) have recently published the X-ray structure of the Δ^{9-11} derivative of (I). Both those compounds display catemeric carboxyl-to-ketone hydrogen bonding, and we report here that (I) also adopts this hydrogen-bonding mode in the solid state.



(I)

Fig. 1 shows the asymmetric unit, which consists of two molecules, I and I′, which differ principally in the rotation of the carboxyl group about the C9—C10 bond. The substituents at C9, which has an *S* configuration, are staggered with respect to those at C2, so that the methyl group is *anti* to C1; the C1—C2—C9—C11 torsion angle is −178.0 (3)° in molecule I and 179.9 (3)° in molecule I′, a difference of only 2.1 (4)° (Table 1). However, in molecule I, the carboxyl group is rotated so that its C═O group is turned toward the molecular face bearing the angular methyl group, a *cisoid* arrangement, in which the C2—C9—C10—O3 torsion angle is 73.7 (4)°, while in I′, this relationship is *transoid* and the corresponding angle is −123.6 (4)°, a difference of 162.7 (6)°.

The partial averaging of C—O bond lengths and C—C—O angles by disorder often seen in acids occurs only in the carboxyl-pairing hydrogen-bonding mode. As in other catemers, no significant averaging is observed for molecule I, whose bond lengths are 1.193 (4)/1.316 (5) Å, with angles of 124.5 (4)/112.1 (3)°; for molecule I′, these values are 1.190 (5)/1.320 (5) Å and 124.4 (4)/112.4 (4)°. Our own survey of 56 keto acid structures which are not acid dimers gives average values of 1.200 (10)/1.32 (2) Å and 124.5 (14)/112.7 (17)° for these lengths and angles, in accord with typical values of 1.21/1.31 Å and 123/112° cited for highly ordered dimeric carboxyls (Borthwick, 1980). The three methyl groups are fully ordered in molecules I and I′, and atoms C11 and C13 are staggered relative to the substituents at their points of attachment.

Fig. 2 illustrates the packing of molecules I and I′ in the cell, with extracellular molecules included to show the two crystallographically independent single-strand hydrogen-bonding catemers, in which each chain proceeds from the carboxyl group of one molecule to the ketone group of a neighbor of its own type. Among such catemers, the observed prevalence of subtypes, describing the relation of adjacent molecules, is

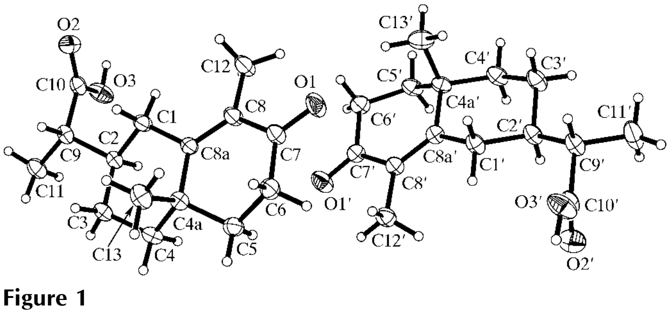


Figure 1
The asymmetric unit of (I) with the atom-numbering scheme. Displacement ellipsoids are shown at the 20% probability level.

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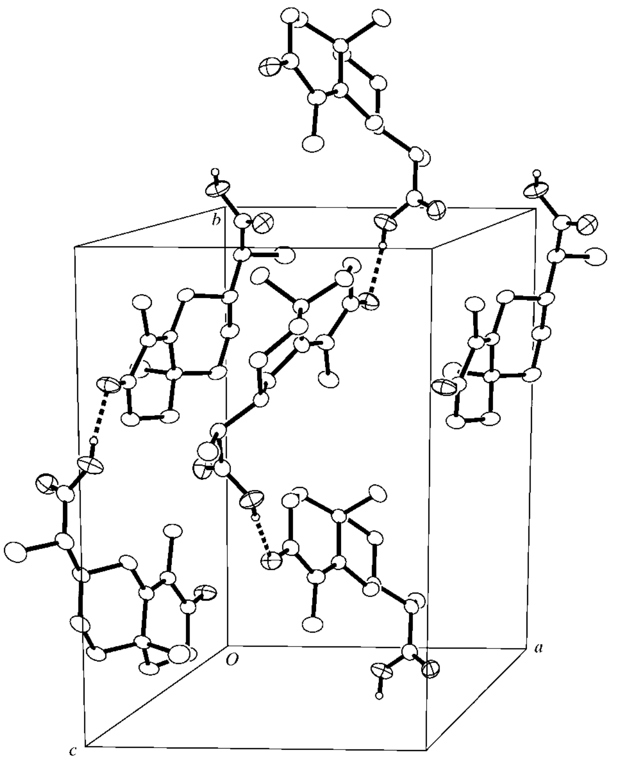

Figure 2
A packing diagram, with extracellular molecules to illustrate the two kinds of single-strand helical catemers proceeding in the *b* direction. Those of type-I follow an axis in the center of the cell at $a = \frac{1}{2}$, while those of type-I′ follow an axis in the *bc* face. Methylene and methine H atoms have been omitted for clarity. Displacement ellipsoids are shown at the 20% probability level.

screw > translation > glide. Here, adjacent intrachain units are related by a twofold screw along *b*; helices of type-I follow an axis through the cell center, while the axis for the counter-directionally aligned type-I′ helices lies in the *bc* face of the chosen cell.

Consistent with the difference found between molecules I and I′ for the rotation of the COOH group about C9—C10, the intramolecular ketone *versus* carboxyl dihedral angles for I and I′ differ by only 11.04 (14)°. The intermolecular ketone *versus* carboxyl dihedral angles for adjacent hydrogen-bonded molecules are also similar, with a value of 65.06 (15)° for the type-I chains and 57.67 (15)° for the type-I′ chains.

Considering the difference of 162.7 (6)° in carboxyl rotation, the geometry of the hydrogen bonding itself for I *versus* I′ adheres remarkably closely to standard patterns for O—H···O═C situations. We characterize the geometry of hydrogen bonding to carbonyls using a combination of the H···O═C angle and the H···O═C—C torsion angle. These describe the approach of the H atom to the O atom in terms of its deviation from, respectively, C═O axiality (ideal = 120°) and planarity with the carbonyl group (ideal = 0°). In molecule I, these angles are 119.9 (13) and −14 (2)°, respectively, while in molecule I′, they are 122.9 (13) and 16 (2)°, respectively.

Three intermolecular C—H···O close contacts exist, all for the type-I carboxyl C═O group, within the 2.7 Å range we usually employ for non-bonded C—H···O packing interactions (Steiner, 1997). These involve H5′*B* (2.63 Å) and H6′*B* (2.65 Å) within the same type-I′ molecule, part of a unit related translationally in *a*, plus H6*B* (2.59 Å) in a type-I molecule, its own hydrogen-bonding partner, screw related in *b*. Using compiled data for a large number of C—H···O contacts, Steiner & Desiraju (1998) find significant statistical directionality, even as far out as 3.0 Å, and conclude that these are legitimately viewed as 'weak hydrogen bonds', with a greater contribution to packing forces than simple van der Waals attractions.

The KBr IR spectrum of (I) displays absorptions at 1726 and 1627 cm^{-1}, consistent with known hydrogen-bonding shifts due, respectively, to its removal from acid C═O and its addition to an unsaturated ketone; a minor peak appears at 1675 cm^{-1} and a shoulder appears at *ca* 1599 cm^{-1} (C═C). In $CHCl_3$ solution, where dimers predominate, the major peaks appear, more normally, at 1708 and 1656 cm^{-1}, with a smaller C═C peak at 1608 cm^{-1} and a typical carboxyl-dilution shoulder near 1750 cm^{-1}.

Experimental

Commercial (−)-*α*-santonin of known relative and absolute stereochemistry (Barton *et al.*, 1962; Nakazaki & Arakawa, 1962; Asher & Sim, 1965; Coggin & Sim, 1969) was obtained from the Aldrich Chemical Co., Milwaukee, Wisconsin, USA, and subjected to the Li/NH_3 reductive procedure described by Bruderer *et al.* (1956) and Howe *et al.* (1959), who have also assigned the optical rotation. Crystals of (I) (m.p. 398 K) were obtained from an acetone–water solution.

Crystal data

$C_{15}H_{22}O_3$
$M_r = 250.33$
Monoclinic, $P2_1$
$a = 10.0225$ (14) Å
$b = 14.862$ (2) Å
$c = 10.0873$ (14) Å
$\beta = 110.758$ (11)°
$V = 1405.0$ (3) Å^3
$Z = 4$

$D_x = 1.183$ Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 25 reflections
$\theta = 4.5$–13.8°
$\mu = 0.08$ mm^{-1}
$T = 296$ (2) K
Parallelepiped, colorless
0.44 × 0.30 × 0.22 mm

Data collection

Siemens *P*4 diffractometer
$2\theta/\theta$ scans
5441 measured reflections
2579 independent reflections
1977 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.029$
$\theta_{\max} = 25.0°$

$h = -11 \rightarrow 11$
$k = -17 \rightarrow 17$
$l = -11 \rightarrow 11$
3 standard reflections every 97 reflections intensity variation: <1.5%

Table 1
Selected geometric parameters (Å, °).

O2—C10	1.193 (4)	O2′—C10′	1.190 (5)
O3—C10	1.316 (5)	O3′—C10′	1.320 (5)
O2—C10—C9	124.5 (4)	O2′—C10′—C9′	124.4 (4)
O3—C10—C9	112.1 (3)	O3′—C10′—C9′	112.4 (4)
C1—C2—C9—C11	−178.0 (3)	C1′—C2′—C9′—C11′	179.9 (3)
C2—C9—C10—O3	73.7 (4)	C2′—C9′—C10′—O3′	−123.6 (4)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O1^{i}	0.87 (4)	1.91 (5)	2.752 (4)	161 (4)
O3′—H3′···O1′^{ii}	0.82 (5)	1.88 (5)	2.682 (4)	168 (4)

Symmetry codes: (i) $1 - x, y - \frac{1}{2}, 1 - z$; (ii) $2 - x, \frac{1}{2} + y, 1 - z$.

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.042$
$wR(F^2) = 0.105$
$S = 1.03$
2579 reflections
337 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0451P)^2 + 0.1708P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.14$ e Å^{-3}
$\Delta\rho_{\min} = -0.10$ e Å^{-3}

The H atoms of molecules I and I′ were found in electron-density difference maps but were placed in calculated positions (0.96 Å for methyl, 0.97 Å for methylene and 0.98 Å for methine H atoms) and allowed to refine as riding models on their respective C atoms. The displacement parameters were fixed at 120% of those of their respective C atoms, except for the methyl H atoms, which were fixed at 150% of those of their respective C atoms. The postitional parameters of the carboxyl H atoms were allowed to refine, but their displacement parameters were fixed at 0.08 Å^2. The absolute configuration was not directly determined and Friedel pairs were averaged.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1365). Services for accessing these data are described at the back of the journal.

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